



E1923
JACC April 5, 2011
Volume 57, Issue 14



PHASE 1, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL EVALUATING THE ANTIPLATELET EFFECTS OF NAPROXEN AND ESOMEPRAZOLE MAGNESIUM (VIMOVO™) AND CONCOMITANT LOW-DOSE ASPIRIN

i2 Poster Contributions

Ernest N. Morial Convention Center, Hall F

Monday, April 04, 2011, 3:30 p.m.-4:45 p.m.

Session Title: Pharmacotherapy - Interventional Aspects

Abstract Category: 21. Pharmacotherapy - Interventional Aspects

Session-Poster Board Number: 2514-506

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Background: Low-dose aspirin (LDA) and nonsteroidal antiinflammatory drugs (NSAIDs) may be used concomitantly in patients with arthritic conditions and cardiovascular risk. There is evidence that some NSAIDs may interfere with platelet inhibition by LDA. Therefore, the impact of a fixed-dose combination (FDC) of enteric-coated (EC) naproxen 500mg and immediate-release esomeprazole magnesium 20mg on antiplatelet action of LDA was investigated.

Methods: Phase 1, single-center, double-blind, placebo-controlled, parallel-group study. Healthy adults (aged 50-75 years) received EC LDA 81mg once daily on Days 1-5 then were randomized to receive LDA plus either naproxen/esomeprazole or placebo twice daily on Days 6-10. Serum thromboxane B2 (TXB2) levels (specific marker of LDA-induced effects on platelet cyclo-oxygenase-1 [COX-1] activity) were assessed on Days 1 and 6 (pre-dose), and Day 11. The primary endpoint was % TXB2 inhibition from Day 1 to Day 11. The primary analysis included subjects with $\geq 95\%$ TXB2 inhibition at Day 6 vs Day 1 and TXB2 data at Day 11. Non-inferiority was concluded if the lower limit of 90% confidence interval (CI) in % inhibition exceeded 90.0%.

Results: Of 42 subjects randomized (mean age 60 ± 7 years), 32 were evaluable. Key data are summarized in the Table. The 90% CI lower limits around % TXB2 inhibition from Day 1 to Day 11 exceeded 90.0% for both groups.

Conclusions: The effect of FDC naproxen/esomeprazole on COX-1 inhibition by LDA is non-inferior to LDA alone in healthy subjects.

TXB2 inhibition in subjects treated with LDA plus naproxen/esomeprazole magnesium or placebo		
	LDA + naproxen/esomeprazole magnesium (N=14)	LDA + placebo (N=18)
Mean TXB2 concentration (pg/mL)		
Day 1	10127.6	5644.9
Day 6	38.5	21.0
Day 11	15.1	13.3
Mean % inhibition (SD) from Day 1 to Day 6 [90% CI]	99.2 (0.8) [98.8, 99.6]	98.8 (1.3) [98.2, 99.3]
Mean % inhibition (SD) from Day 1 to Day 11 [90 % CI]	99.6 (0.5) [99.4, 99.8]	99.1 (1.1) [98.7, 99.6]